REMARKS

Restriction

SEQ ID NOS. 1, 3, 5, and 7 all code for proteins with manillase (hyaluronidase) properties. See, specification, Page 6, lines 5-7. The attached sequence alignment (Exhibit 1) shows that the amino acid sequences are highly related, sharing at least about 93% identity (about 454/488) between all four isoforms, with high sequence identity between the individual pairs. In a teleconference with Examiner Patterson, it was agreed that Applicant would submit such evidence for his consideration. In view of this submission, it is requested that the restriction between the various forms be withdrawn.

Sequence

The specification has been amended to conform to the sequence rules by adding sequence identifiers to the unidentified sequences. These sequences were already listed in the sequence listing filed February 4, 2003.

Rejection under §101

Claim 20 has been amended to conform with U.S. practice. Support for the amendment can be found throughout the specification, including Page 2, line 27-Page 4, line 9.

Rejections under §112, second paragraph

Claim 16 has been amended to a pharmaceutical composition. Support for the amendment can be found throughout the specification, including Page 6, lines 25-26.

Claims 7, 18, and 19 have been amended to clarify them; these amendments do not change the claim scope, but merely clarify what the skilled worker would have understood from the claim's original wording.

Rejections under §102

It is believed that amendment to claim 18 renders this rejection moot.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

Richard M. Lebovitz, Reg. No. 37,067
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-2332

Date: August 23, 2004

EXHIBIT

1

CLUSTAL W (1.82) multiple sequence alignment

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SEQIDNO1.       KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
SEQIDNO7.       KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGPWSFVNITSPKLFKLLEGLSPGYFRV 60
SEQIDNO3.       KEIAVTIDDKNVIASASGSFLGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
SEQIDNO5.       KEIAVTIDDKNVIASASESFHGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
                ***************.* ** ************ ****:********************

SEQIDNO1.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETEDDLVKLTKG 120
SEQIDNO7.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDDLVKLTKG 120
SEQIDNO3.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120
SEQIDNO5.       GGTFANRLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120
                ****** ****************************************** *:*******

SEQIDNO1.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO7.       SKMRLLFDLNAEVRTGYEIGKKTTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO3.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO5.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNGPDHTS 180
                ********************** ******************************** *****

SEQIDNO1.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240
SEQIDNO7.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSPVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240
SEQIDNO3.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSXVKGLADEAGDHVTAFTL 240
SEQIDNO5.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADEAGDHVTAFTL 240
                ****************************** ************ ****** *** ******

SEQIDNO1.       HQYYFDGNTSDVSTYLDATYFKKLQQLFDKVKDVLKNSQHKDKPLWLGETSSGYNSGTKD 300
SEQIDNO7.       HQYYFDGNTSDVSTYLDASYFKKLQQLFDKVKDVLKNSPHKDKPLWLGETSSGCNSGTKD 300
SEQIDNO3.       HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDEPLWLGETSSGYNSGTED 300
SEQIDNO5.       HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDKPLWLGETSSGYNSGTED 300
                ************* ****:*******************:* ***:********** ****:*

SEQIDNO1.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO7.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO3.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO5.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYSGYYGPLDKNTLEPNPDYWLMHVHNSLV 360
                ********************************.**** ***********************

SEQIDNO1.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIDQYGG 420
SEQIDNO7.       GNTVFKVDVGDPTNKTRVYAQCTKTNSKHTQGKYYKGSLTIFALNVGDEEVTLKIDQYGG 420
SEQIDNO3.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDGDVTLKIGQYSG 420
SEQIDNO5.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIGQYSG 420
                *********.*****:***************.:*************** :*****.**.*

SEQIDNO1.       KKIYSYILTPEGGQLTSQKVLLNGKELKLVSDQLPELNANESKTSFTLSPKTFGFFVVSD 480
SEQIDNO7.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480
SEQIDNO3.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480
SEQIDNO5.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPQLNADESKTSFTLSPKTFGFFVVSD 480
                ****************************:********:***:********************

SEQIDNO1.       ANVEACKK 488
SEQIDNO7.       ANVEACKK 488
SEQIDNO3.       ANVEACKK 488
SEQIDNO5.       ANVEACKK 488
                ********
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CLUSTAL W (1.82) multiple sequence alignment


SEQIDNO1.       KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
SEQIDNO7.       KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGPWSFVNITSPKLFKLLEGLSPGYFRV 60
SEQIDNO3.       KEIAVTIDDKNVIASASGSFLGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
SEQIDNO5.       KEIAVTIDDKNVIASASESFHGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
                ***************.* ** ************ ****:********************


SEQIDNO1.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETEDDLVKLTKG 120
SEQIDNO7.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDDLVKLTKG 120
SEQIDNO3.       GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120
SEQIDNO5.       GGTFANRLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120
                ****** ****************************************** *:*******


SEQIDNO1.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO7.       SKMRLLFDLNAEVRTGYEIGKKTTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO3.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180
SEQIDNO5.       SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNGPDHTS 180
                ********************** ******************************** *****


SEQIDNO1.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240
SEQIDNO7.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSPVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240
SEQIDNO3.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSXVKGLADEAGDHVTAFTL 240
SEQIDNO5.       AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADEAGDHVTAFTL 240
                ****************************** *********** ****** *** ******


SEQIDNO1.       HQYYFDGNTSDVSTYLDATYFKKLQQLFDKVKDVLKNSQHKDKPLWLGETSSGYNSGTKD 300
SEQIDNO7.       HQYYFDGNTSDVSTYLDASYFKKLQQLFDKVKDVLKNSPHKDKPLWLGETSSGCNSGTKD 300
SEQIDNO3.       HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDEPLWLGETSSGYNSGTED 300
SEQIDNO5.       HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDKPLWLGETSSGYNSGTED 300
                ************* ****:*****************:* ***:********** ****:*


SEQIDNO1.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO7.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO3.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360
SEQIDNO5.       VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYSGYYGPLDKNTLEPNPDYWLMHVHNSLV 360
                ********************************.**** **********************


SEQIDNO1.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIDQYGG 420
SEQIDNO7.       GNTVFKVDVGDPTNKTRVYAQCTKTNSKHTQGKYYKGSLTIFALNVGDEEVTLKIDQYGG 420
SEQIDNO3.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDGDVTLKIGQYSG 420
SEQIDNO5.       GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIGQYSG 420
                *********.*****:***************.:*************** :*****.**.*


SEQIDNO1.       KKIYSYILTPEGGQLTSQKVLLNGKELKLVSDQLPELNANESKTSFTLSPKTFGFFVVSD 480
SEQIDNO7.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480
SEQIDNO3.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480
SEQIDNO5.       KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPQLNADESKTSFTLSPKTFGFFVVSD 480
                ****************************:*******:***:********************


SEQIDNO1.       ANVEACKK 488
SEQIDNO7.       ANVEACKK 488
SEQIDNO3.       ANVEACKK 488
SEQIDNO5.       ANVEACKK 488
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